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TRANSACTIONS

OF THE

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TRANSACTIONS

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SOCIETY OF TROPICAL MEDICINE AND HYGIENE.

JANUARY, 1912.

VOLUME V. No. 3.

Proceedings of a Meeting of the Society on Friday, December 15th, 1911, Sir WILLIAM LEISHMAN, F.R.S., *President*, in the Chair.

DEMONSTRATION OF ACID-FAST GERMS CULTIVATED FROM CASES OF LEPROSY.

By H. BAYON,

Cragg's Investigator, London School of Tropical Medicine.

The first attempt to cultivate the germ of leprosy was made several years ago by Sir PATRICK MANSON, who sealed up the serum of a leper in a little glass tube, placed it inside an egg and put it under a hen to hatch. At that time aniline stains had not yet been applied to the staining of bacteria, so there was no possibility of determining the identity of the result. HANSEN also tried to cultivate the germ under a cover-slip, but came to the conclusion that the resulting streptothrix was a contamination. Later on we have the results of BORDONI-UFFREDUZZI and a host of others, making up a total of over thirty names, and notwithstanding this goodly array it is generally admitted that the germ of leprosy has not yet been cultivated.

In the course of time a great deal of reliable evidence has accumulated pointing to the conclusion that leprosy must be due to a streptothrix capable of breaking up into a diphtheroid and acid-fast bacillary form. A streptothrix breaking up into acid-fast rods has been even described as

causing disease in a human being by LEISHMAN and BIRT, moreover we know that the germ of diphtheria is capable of showing definite branching forms under certain circumstances. I unfortunately cannot go fully into the matter at the present moment, but it is sufficient to say that KEDROWSKY has cultivated from two cases of leprosy a streptothrix which caused leprosy-like lesions on injection into animals, and regained the germ as an acid-fast rod.

On beginning my researches on leprosy, I soon noticed that the paramount, and in fact the only difficulty with the bacteriology of leprosy, was not in cultivating germs from the nodules of the patients, but in proving the relationship of the germs so cultivated to the disease itself.

Not only are acid-fast germs ubiquitous, but the methods of identification at our disposal are very incomplete. The smegma "bacillus," so-called, is present on the body surface of every human being, diphtheroids and streptothrices are even more numerous. By injecting a culture of the smegma germ into a rabbit, I was able to produce in a most striking fashion the clinical appearances of leprosy, *i.e.*, nodules in the skin and around the sciatic nerve. In other cases I got the exact microscopical lesions seen in leprous nodules by the injection of human and avian tubercle into the rabbit. To add to my dismay it soon was evident that dead or alive the acid-fast germs of the tubercle group are capable of producing similar lesions. In other words an autoclaved tubercle culture succeeds in giving rise to appearances undistinguishable from those set up by the living germ, except in so far, that of course the dead bacilli are incapable of multiplying.

Serological methods did not appear at first to be able to distinguish the various acid-fasts except in rough groups, but after several attempts I got a definite, specific, clear reaction with leper serum by means of the complement deviation test. On linking up this serum with KEDROWSKY'S germ it reacted in dilutions up to $\frac{1}{100}$, whilst DUVAL'S germ, which was tried in the same time ceased to react at $\frac{1}{5}$.

I then turned my attention to the germs that I had cultivated from a case of leprosy and found that the streptothrix I had got from the nodules turned acid-fast on injection into a rat, and I found that I could produce identical leprous lesions, whether I injected the streptothrix, the acid-fast rod stage or the ground-up nodules of a leper. I was able to satisfy myself as fully as our methods go that the germ I had

cultivated was the one causing the disease of the patient, for a bacillary extract (not a vaccine) caused a typical, definite rise of temperature on injection. Of course it is quite possible that leprosy in different parts of the world is caused by different germs, but so far I have been unable to cause anything similar to leprosy by the injection of DUVAL'S germ.

I believe that now, as a result of my animal and serological experiments, I am able to state that a definite streptothrix is the cause of leprosy, and that it can be identified by animal experiment and serological tests.

You will have to judge these claims from the slides and cultures I am going to demonstrate.

DEMONSTRATION.

Cultures of KEDROWSKY'S, ROST'S, DUVAL'S, CAMPANA'S germs of leprosy.

Diphtheroid cultivated from a leper at the London School of Tropical Medicine.

Series of 22 acid-fast germs from various sources.

Microscopical sections of rats and rabbits injected with human lepra cultures.

Sections from rats with genuine, spontaneous rat leprosy.

NOTE ON AN INVESTIGATION ON THE CAUSATION OF EPIDEMIC DROPSY IN CALCUTTA.

BY

MAJOR E. D. W. GREIG, M.D., D.Sc., I.M.S.

In December, 1909, I was deputed by the Government of India to conduct an enquiry into the causation of a severe outbreak of epidemic dropsy in Calcutta. The results of my investigations have been embodied in two reports, the first* has been published and the second† report is in the press. I propose to state very shortly the main conclusions arrived at, and have forwarded lantern slides, which will illustrate the points dealt with.

The evidence appears to warrant the following conclusions :—

1. That no *causa morbi* is to be found in the blood, œdematous fluid, excreta, etc., of epidemic dropsy cases.

2. That the features of epidemic dropsy very closely resemble those of "Ship Beri-Beri," as described by AXEL HOLST, and the cases present also symptoms of scorbutus. The number of red blood corpuscles is diminished during the course of the disease. The percentage of hæmoglobin is reduced. There is a relative increase of the lymphocytes (small mononuclears). The coagulation time is not appreciably increased.

3. That the evidence points to epidemic dropsy being non-infectious.

4. That there is evidence to show that epidemic dropsy is a nutritional disease, and is brought about by a "one-sided" dietary.

5. That a community (Marwaris), living in the heart of the affected part of Calcutta, practically escaped epidemic dropsy. A careful analysis of their dietary, which differs materially from that of the Bengalis,

* Scientific Memoirs of the Government of India. No. 45. 1911.

† Ditto. (In the Press)

shows that it is much richer in some important constituents—*e.g.*, phosphorus, than a rice dietary, and therefore, the quantity of these constituents taken by the Marwaris, amongst whom no fatal cases of epidemic dropsy have been recorded, is greater than that consumed by Bengalis, whose staple is rice, and who were severely affected by epidemic dropsy in the recent outbreak. The better class European community in Calcutta, living on a mixed dietary, and not consuming large quantities of rice continuously, have escaped.

6. That the effect of the addition of meat to a dietary is very marked; amongst non-meat-eaters, Hindu widows, who for religious reasons, are prevented from consuming meat, showed the highest mortality from epidemic dropsy, and the lowest mortality was amongst Hindu males and the percentage of meat-eaters amongst the latter is high. Hindu children have approximately the same percentage of meat-eaters amongst males and females, and the mortality from epidemic dropsy is approximately the same in the two sexes in children.

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7. That chemical analysis and histological examination show that by the process of "polishing," as carried out in the steam and other mills in Calcutta and elsewhere, constituents essential for nutrition are removed from the rice, and that the ata (wheat) which many Bengalis consume habitually, had been so finely sifted that it is deprived of these constituents to an even greater extent than rice.

8. That the chemical examination of samples of the kind of rice habitually consumed by patients affected by epidemic dropsy shows that the samples had undergone a process of "polishing" by steam milling, and that important constituents had been removed to a considerable extent; that wheat consumed by patients affected by epidemic dropsy had undergone a considerable loss of phosphates in the preparation of ata.

9. That pigeons show, when fed on "polished" rices, both boiled and unboiled, a progressive loss of weight with characteristic polyneuritis. Chemical analyses of these samples of rice show them to have a low phosphorus content.

10. That control pigeons when fed on a mixture of wheat and pulses show no loss of weight, but rather a gain, and they have remained under

http://www.archive.org/details/n3transactionsof05roya

observation in good health for months. Chemical analysis of this food shows that it contains double the quantity of phosphorus contained in the sample of rice used for feeding the pigeons.

11. That the two severe outbreaks of epidemic dropsy in Calcutta and Bengal, namely in 1877-78-79 and in 1907-08-09, have been correlated with a sustained high price of food grains during the period, and the cessation of these epidemics has synchronised with the fall in the price of food.

12. The sections of the community in Calcutta with a small fixed income, *i.e.*, clerks, petty traders, etc., show the highest morbidity from epidemic dropsy in Calcutta.

13. The epidemic is brought about in times of high price of food by the fact that a section of the population with a small fixed income is, on account of this rise, obliged to abandon the purchase of adequate supplementary articles of dietary, and, consequently, the diet becomes dangerously "one-sided"; with the drop in the price of food the income of this class admits of the obtaining of sufficient supplementary articles, and the diet ceases to be "one-sided" and the epidemic terminates.

Appended are Tables showing results and analyses :—

TABLE I.

SHOWING THE RELATIVE FREQUENCY OF SYMPTOMS OF SCORBUTUS IN EPIDEMIC DROPSY.

No. of cases examined.				No. of cases showing Bleeding from Gums and Hæmorrhage of Bowels.			
Adults.		Children.		Adults.		Children.	
Male.	Female.	Male.	Female.	Male.	Female.	Male.	Female.
249	241	23	15	27	18	3	1

Table II.

Showing results of Blood Counts in Epidemic Dropsy.

Age.	Sex.	Race.	Stage of disease.	R.B.C.	Hb°/₀	W.B.C.	P.N.	S.M.	L.M.	E.
15	F.	I. Ch.	Chronic (relapse)	3,540,000	48	4,500	56	31	12	1
14	F.	,,	,, ,, ...	3,580,000	48	4,000	41	50	8	1
15	F.	,,	,, ,, ...	4,590,000	56	5,000	50	32	18	0
15	F.	,,	,, ,, ...	4,020,000	57	5,000	50	44	5	0
14	F.	,,	,, ,, ..	4,670,000	60	5,000	63	29	8	0
15	F.	,,	,, ,, ...	4,780,000	65	9,000	71	21	9	0
24	F.	,,	,, ., ...	4,990,002	62	8,000	52	39	7	0
15	F.	,,	,, ,, ...	4,590,000	56	5,000	50	32	12	0
33	M.	,,	,, ,, ...	3,200,000	55	8,000	65	21	14	0
35	M.	B.	,, ,, ...	3,740,000	40	5,500	58	34	17	1
28	M.	B.	,, ,, ...	3,650,000	55	9,000	52	36	12	0
24	F.	I. Ch.	Acute	2,200,000	32	7,812	72	13	15	0
25	F.	,,	,, ...	3,910,000	60	9,000	58	30	12	0
19	F.	,,	Chronic	3,350,000	50	12,000	78	8	14	0
15	M.	B.H.	,, ...	4,000,000	42	5,000	65	26	8	1
55	M.	,,	,, ...	3,940,000	35	12,000	62	25	12	1
29	M.	,,	Acute	2,100,000	14	6,700	—	—	—	—
22	M.	M.	Chronic	3,800,000	60	5,600	60	34	6	0
45	F.	I. Ch.	Convalescent ...	5,020,000	80	7,000	65	27	8	0
16	F.	,,	,,	4,850,000	70	6,000	43	48	5	2
16	F.	Brahmo	,,	5,110,000	78	7,000	57	38	5	0
22	F.	,,	,,	4,420,000	75	5,000	37	48	13	2

Table III.

ANALYSIS OF ARTICLES OF MARWARI DIET.

	Moisture %	Ash %	Albuminoids %	Phosphoric Acid %
Wheat	13·7	1·7	12·1	0·73
Bajri	11·5	2·5	10·4	0·78
Basan	13·8	3·2	23·6	0·84
Dal	14·6	3·2	22·2	0·95
Papar	18·8	6·5	21·9	0·85
Kair	18·5	4·2	16·8	0·57
Sangar	16·0	4·1	17·1	0·54
Gourfali	18·0	8·1	17·1	0·76
Motha-ka-fali	16·0	5·5	20·1	1·10

From the quantity of the articles consumed in the diet the amount of phosphorus ordinarily taken per day by Marwaris has been calculated as follows :—

		Grains Phosphoric Anhydride.
Rice	½ to 1 chittak	1·8 to 3·6
Wheat Ata ...	7 to 8 ,, ...	46·0 to 52·5
Bajri Flour ...	3 to 4 ,, ...	21·0 to 28·0
Dal	½ to 2 ,, ...	4·3 to 28·0
Basan	½ chittak	3·75 to 3·75
		76·85 115·85

Table IV.

SHOWING THE AMOUNT OF PHOSPHORUS ORDINARILY TAKEN PER DAY BY BENGALIS.

	Diet 1.		Phosphoric Anhydride.
Morning Meal	Rice ... 3½ chittaks		13·54 grains.
	Dal ... ½ chittak		2·49 ,,
Evening Meal	Rice ... 3 chittaks		11·61 ,,
	Dal ... ½ chittak		2·49 ,,
		Total ...	30·13 ,,
	Diet II.		
Morning Meal	Rice ... 3½ chittaks		13·54 ,,
	Dal ... ½ chittak		2·49 ,,
Evening Meal	Ata ... 3 chittaks		7·02 ,,
	Dal ... ½ chittak		2·49 ,,
		Total ...	25·54 ,,

TABLE V.

SHOWING PROPORTION OF PHOSPHORUS IN WHEAT FLOUR.

Calcutta Milled Wheat.	Moisture %	Ash %	Phosphoric Anhydride
Ata wheat No. 4, entire grain	11·86	1·13	0·59
Ata (wheat) No. 2.	11·93	0·60	0·32
Ata (wheat) B	12·53	0·33	0·21
Wheat Bran	13·33	4·20	2·02
Soojee, small	13·06	0·66	0·26
,, large	13·00	0·60	0·22
Flour, 3	12·33	0·53	0·22
,, 2	12·93	0·53	0·21
,, 1	11·46	0·53	0·20

PELLAGRA IN NYASALAND.

BY

HUGH S. STANNUS, M.B., LOND.

I may preface my remarks on pellagra in Nyasaland by saying that this communication contains no fresh discovery in the field of pathogeny, but rather is an account of some of the difficulties in diagnosis which I experienced before arriving at the conclusion that I was dealing with that disease. It will therefore be of more interest possibly to those who, like myself, are isolated in various parts of Africa or elsewhere, who have never seen the disease, and for whom I think it is very difficult to conjure up the picture of the disease as it might be found among native races from text-book descriptions of the affection as seen in Europeans.

As far as I am aware, with the exception of Lower Egypt, Algiers and the Red Sea Coast, pellagra has been practically unknown in Africa.

BALFOUR says: "It is unknown in the Sudan." SANDWITH saw a few cases on Robben Island, but no others have been described from South Africa. The same is true of West Africa, with the possible exception of a single case reported to SAMBON in a private letter.

The discovery therefore of cases in Nyasaland is of some interest, and the same problem presents itself for solution as has confronted American epidemiologists in dealing with the recent appearance of the disease in the United States, namely, how far can the appearance of the disease be said to be due to fresh introduction or extension, and how far due simply to recognition of the affection?

Recognition depends largely on the type of the affection and opportunity for making observations. SAMBON has remarked how at the present time the disease is said to have disappeared from parts of Southern Europe, whereas the truth is only that the disease is less easily recognised, and that unless special search is made for cases opportunity for seeing them is small.

I cannot help thinking that for similar reasons pellagra has escaped recognition among the native inhabitants over so large an area of Africa in the past.

In 1910, while stationed at Zomba, the administrative headquarters of Nyasaland, my attention became drawn to a number of inmates of the central native prison, who presented a condition at the angles of the mouth, somewhat resembling the conditions seen in syphilis, known as rhagades. Investigation showed this condition to be commonly associated with changes in the surface of the tongue, producing a smooth condition devoid of papillæ. Some of the cases showed general symptoms, to be referred to later, viz., anæmia and digestive troubles, but for some time they did not present any further signs of the disease. Then several of these natives developed an affection of the skin on various parts of the body. For many months, failing to recognise this eruption, I was at a loss to explain the condition, and it was not until the eruption recurred in some apparently cured cases shortly before I left the country, while other patients developed paretic symptoms, that the identity of the disease dawned upon me.

The natives themselves apparently recognise the affection and make use of the word "chocho," indicating, I think, the skin eruption, and the condition of the lips and tongue.

Dealing with the etiology, 40 cases occurred in sixteen months among the inmates of the central prison, who totalled an average of 200.

The patients were all natives of Nyasaland, that is Africans of Bantu stock, most tribes of the Protectorate being represented.

Cases occurred among young adults and old men without distinction, and among old inmates and those recently immured.

No case was seen among eight female prisoners under observation at the same time, nor did any of twelve male lunatics under care in an institution, distant a quarter of a mile from the prison, show any rash or other definitely pellagrous symptoms.

These prisoners were housed in cells in batches of ten, the women occupying an adjoining cell.

Cases were scattered among the various batches of men.

The cells in which they spent the night were of brick with white-washed walls and cement floors, forming the sides of a large walled-in square, situated in the middle of a cleared area 200 acres in extent, on the lower slopes of Zomba mountain, through which several rapidly flowing stony streams flowed.

These prisoners were employed in gangs, some in road-making,

stream-clearing, carrying wood, others in transporting building materials, and others, as were also the women, in grass-cutting.

Their food consisted of rice, salt, and a certain amount of fish and beans, together with green vegetables and other little things which their relations were allowed to bring them.

During the first part of the period they were under observation, they were clothed in calico loin-cloths and a variety of upper garments, more or less on the principle of a short-sleeved shirt. During the latter part of the period, they wore sacking cloth usually over their own calico, and a loose sacking vest worn by most next to the skin. The women during the whole of the period wore calico, native fashion, that is, exposing the body above the middle of the breasts.

Cases apart from these in the prison have been but rarely seen, and have been very mild.

Minor ailments among the prisoners are treated by Indian hospital assistants resident at the prison, and it is significant that a large number of cases had been returned as eczema, and that the cases I afterwards pronounced as pellagra had been so labelled.

I am unable to give any very definite statement as to seasonal variations, but as far as I could determine it appeared that most cases occurred in April and October.

Of the symptoms, the affection of the skin is pre-eminent. Firstly, I should like to lay stress on the almost constant occurrence of the rhagades-like soreness at the muco-cutaneous borders at the corners of the mouth; a similar condition was often seen affecting the free margin of the prepuce, the skin in these situations being thrown into sodden folds of a greyish colour.

These signs appear early in the disease and may persist for many months before the characteristic dermatitis makes its appearance, which, indeed, I believe is often delayed a season.

Commonly associated however with these are the changes in the tongue. The dorsum at first covered by heaped-up sodden epithelium later becomes denuded, sometimes not equally, giving a variegated appearance, but going on to completion so that the surface is of a shining bright pink colour devoid of papillæ.

The skin eruption is characterised by site, mode of extension and exact symmetry. Most commonly it is first seen on the extensor

surfaces of the forearms, patches then appear in the triangles of the neck, on the cheeks, nose and forehead, the dorsum of the hands and outer aspects of the upper arms, dorsum of feet and shins.

Some or all of these areas are involved and extension is variable in amount, so that in a marked case the whole of the outer aspects of the upper limbs, the dorsum of the hands, the whole of the neck except a triangular area beneath the chin with the apex at the pomum adami, the scapular regions behind, the upper part of the chest in front, more especially in the mid-line, the cheeks, nose, forehead, and upper surfaces of the pinnæ, the dorsum of the feet and shins are all affected.

These areas have been severally referred to by various writers as the "necklace" area, the "butterfly" area, the "mask," the "cravat" area, etc.

Less commonly the skin of the scrotum was implicated, and in one case the adductor aspects of the thighs.

The eruption does not appear synchronously in all these situations, but fresh patches may appear each week: one is, however, struck by the symmetry preserved.

The character of the exanthem as observed in natives is distinctive, and, I believe, does not resemble any other affection among them. Commencing as a deepening in colour, the skin (normally a dark chocolate) becomes a dead black, at the same time slightly raised: this is quickly followed either by the appearance of fine wrinkling over the affected patch, and desquamation takes place with the production of dirty greyish-white branny scales, or the surface becomes covered with shining, glazed, cracked patches of epidermis, or again, blebs may form, more especially where the skin is softer.

As the margin of the patch extends, the centre may clear or the affected areas may remain in the glazed condition for many weeks before improvement takes place, leaving the skin apparently normal or slightly glossy and atrophic.

Three of the earlier cases in whom the eruption had cleared up relapsed towards the end of the sixteen months I had them under observation; this was just before I left the country.

During the early stages, when only the lips or lips and tongue are affected, gastro-intestinal and other general symptoms may be noted, furred flabby tongue, loss of appetite, dyspeptic symptoms, constipation,

headache, pains in the limbs. Later anæmia, loss of flesh, with general mental and physical debility going on to cachexia occurred in some. Many others, on the other hand, expressed no wish to leave off work, the extent of the rash being no criterion of the severity of other symptoms.

Coming now to the nervous system, headache, mental apathy in some, irritability in others, and moroseness reflected in the facial expression were commonly seen. This sadness of expression and inability to smile are, as has been pointed out by SANDWITH, almost diagnostic. Insomnia was a symptom complained of by a few, and explained by them as due to the persistence of pain in the limbs.

As above mentioned, I should hesitate to associate any of the cases of lunacy with pellagra, and at the same time I may say that in no case presenting undoubted cutaneous features of the disease were frank mental symptoms seen.

Speaking generally, cranial nerve symptoms appear to be rare. In two of my cases amaurosis occurred, in both associated with deafness, the onset being rather sudden and progress rapid, so that in a comparatively few days vision was reduced to light perception, and it was only by shouting that a few words could be conveyed to the patient. They remained in this condition for some weeks, then some improvement began, but had not progressed very far when I left the country.

Opthalmoscopical examination revealed no gross lesions: there was no blurring of the discs or other sign of papillitis. A third patient who complained of partial loss of vision in one eye was found to have marked changes in the fundus as of a choroiditis of syphilitic origin. I mention this case as a similar observation has been recorded from America. Though no primary mydriasis was seen in any case, there was loss of sphincter tone in both the cases just mentioned, as evidenced by the fact that mydriasis persisted for two weeks after the use of atropine drops.

No strabismus was noted in any case.

Apart from the general loss of flesh there was a considerable degree of wasting of the muscles of the calves unassociated with fibrillary twitching.

In the same way muscular power was generally diminished, and in the lower extremities amounted to actual paresis, the patient being unable to stand or walk unsupported; there was, however, no drop-wrist or drop-foot. On attempted movement against resistance the lower

limbs were seized with tremors. The gait was hesitating, the feet kept rather wide apart with a tendency to fall forwards or backwards, but there was no ataxy apart from the static ataxia. It is practically impossible to determine the presence of spasticity as opposed to flaccidity in these native patients.

Subjective sensory phenomena were marked, tingling pains, "pins and needles" and burning pains in the soles of the feet, especially along their outer margins and in the pulps of the toes; pains in the legs, especially in the calves, were an almost constant symptom, and associated with considerable tenderness on pressure of the calf muscles.

Objective changes of sensibility could not be definitely elicited.

The knee-jerks were diminished in some cases, increased in others. It has to be remembered that elicitation among all natives of the plantar reflex is a very difficult matter, and I therefore do not mention the phenomenon.

The bladder and rectum were not affected.

I should like to mention here that at the same time there were two prisoners in hospital exhibiting the subjective sensory symptoms in the lower extremities, above mentioned, but who at no time had any affection of the skin. The tenderness of the toes was exquisite, and accompanied by local cyanosis, coldness and sweating—pointing to involvement of the sympathetic system. They both were anæmic, apathetic, morose, in fact I do not believe they smiled during the whole time I had them under observation, moreover one had diminution of vision, which, as far as could be judged, amounted to a central scotoma in each eye. I think the possibility of these two cases being "pellagra sine pellagra" must be entertained.

Associated with the specific dermatitis, another eruption was seen in ten cases, and also noticed in two other prisoners not suffering from pellagra.

This consists of a folliculitis in which there is retention of secretion, either forming small hemispherical pustules, but more commonly giving rise to a characteristic condition in which the hard dried secretion is partly extruded from the enlarged follicles as little filiform masses, prickly to the touch, each being surrounded by a deep black areola, the little plug of secretion may drop out, leaving a little open pit.

The distribution in six cases in which it was associated with a typical

pellagrous rash was limited to the thighs and buttocks; in other cases in which there was only the affection of lips and tongue it was more extensive, involving the upper and lower extremities, the abdomen and chest. Lesions were most closely massed on the abdomen, the nates and thighs with the exception of the internatal cleft and crutch, the extensor aspects of arms and axillary folds; the back, chest, neck and face were comparatively free.

Such an eruption, as far as I know, has not been described in pellagra, though PROCOPUI mentions a pustular eruption on the face, of an acneiform character, and pustulous inflammations, due probably to secondary infection in the perianal and perineal regions and backs of the hands, have been described.

The disease which I have attempted to describe above, presenting the picture of a toxæmia attacking the nervous system, rendering the skin more liable to irritation by the sun's rays, with the production of a symmetrical characteristic rash of particular distribution recurring in successive years, is, I believe, undoubtedly pellagra.

Lack of time and opportunity prevented me from making more extensive observations, but such will, I feel sure, bring the Nyasaland disease more into line with the disease as known elsewhere, though I think one must admit that local conditions may play a part in the production of variations in type in any disease. Such differences have been noticed in pellagra as seen in Southern Europe, Egypt, and recently in America; and in this connection I should like to refer to the series of cases in Jamaica, reported by STRACHAN in 1888, of what he called malarial peripheral neuritis. His patients complained of impaired vision and hearing, numbness and cramps in the extremities, girdle and joint pains; among other symptoms were trophic changes in the skin, widespread neuritis, altered gait, rare monoplegias, knee-jerks altered in either direction, wasting and contractures of muscles, burning pain in feet, soreness of muco-cutaneous junctions, loss of epithelium of tongue, palms and soles hyperæmic, later pigmented but without typical dermatitis.

The affection of the skin in pellagra has been said only to occur at those sites exposed to the sun's rays, and this is no doubt in great part true—as beautifully demonstrated by SANDWITH—but other situations are undoubtedly involved. According to MERK, it is only within recent years that atypical localisations of the dermatitis have been recognised.

MARIE mentions that pellagrous vulvitis has long been recognised, and the affection of the prepuce has also been noted. In view of these facts and of certain of the symptoms of my own cases, I think STRACHAN'S cases may well have been pellagra.

Though I have no pathological material of my own, many of the symptoms described by myself and others are suggestive of a peripheral nerve lesion: such are muscular tenderness, subjective pain in feet, etc. In addition the amaurosis and deafness suggest multiple involvement of cranial nerves comparable to these other symptoms. Without asserting that there is a definite peripheral neuritis, and while accepting pathological findings as far as they go, I think it is probable that, apart from cord lesions, there is involvement of the posterior roots. Taking into consideration the diffuse nature of the cord lesions and the absence of systematisation, it would seem probable that the nervous lesions are produced by a toxin entering the theca by the lymphatic spaces of the posterior roots, setting up a posterior leptomeningitis and then invading the cord.

On the subject of actual causation I do not intend to speak, but for those who will enter the lists of discussion I would recapitulate the following points relating to my cases:—

The staple diet was rice; maize was only rarely eaten; food was periodically examined, and though occasionally damaged grain may have been eaten, such could not often occur.

I am unhappily not in a position to give a detailed account of the insect fauna, possible carriers of protozoal infections, but I may mention that bugs, fleas, lice, tabanids, hæmatopota, stomoxys, mosquitoes and midges are all found in the neighbourhood. Simulidæ of as yet undetermined species are found in Nyasaland, but I am unable to give their distribution. The nature of the country, however, on the lower mountain slopes with swiftly flowing streams would certainly favour their breeding.

PELLAGRA IN THIRTY-FIVE STATES OF AMERICA.

(Illustrated by the Epidiascope.)

By F. M. SANDWITH, M.D.

Although I have been interested in pellagra ever since 1893, when I discovered its presence in Lower Egypt, and have occasionally written on the subject, this is only the second time that I have ventured to read a paper upon it before any Society in this country. Upon the first occasion, which was before the inaugural meeting of the Tropical Section of the British Medical Association at Edinburgh in 1898, the abstract of my paper led to no discussion, and room was not found for the lengthy paper in the published accounts of the meeting, so that I had to send it elsewhere. I might have been disappointed with its reception at the meeting, had it not been that three strangers came up to me later to express their certainty that they had seen in tropical countries out-patients in their hospital practice who had exhibited undiagnosed skin eruptions similar to my photographs and water-colour sketches.

I venture to recall this incident, because I have since met with several repetitions of this occurrence, and I have long held the view that pellagra exists in many parts of the world from which it has not yet been reported.

Possibly Dr. Stannus's interesting account to-night of his discovery of the disease in Nyasaland will stimulate others to search for the possible existence of pellagra in those parts of the tropics in which they are working. The audience in 1898 were all unacquainted with the disease, partly because my communication seemed to have been almost the earliest first-hand detailed account of pellagra in the English language. But the discovery of the prevalence of endemic pellagra in the United States has now added to our literature a large number of pamphlets on the subject, besides an American translation from the French of Dr. A. Marie's book on pellagra, with many additions and illustrations furnished by Dr. C. H. Lavinder and Dr. J. W. Babcock, both of whom have been prominent pioneers in awakening the interest

of the medical profession in the United States to the importance of the disease.

In 1907, six medical men in America wrote on pellagra, while in the following year there were thirty-five papers on the subject, and in 1909 and 1910 there were respectively about 150 and nearly 100 publications on pellagra in the United States. The literary flow is continuing in 1911. Nearly 100 of these papers have been forwarded to me, often by the courtesy of the authors, but generally by the kindness of Dr. BABCOCK. With him and with three or four of his colleagues I have had the advantage of personal conversation and of comparing photographs in London. Dr. BABCOCK, under the auspices of the South Carolina State Board of Health, has already succeeded in holding four annual conferences on pellagra, the last of which took place a month ago in the Columbia State Hospital for the Insane. Some of these conferences have been attended by more than 300 medical men and women. The United States Government and the lay press have been and are much interested in the pellagra invasion. The interesting story of the recognition of the disease in the United States has not yet been fully told.

Though known in Mexico (the original home of maize) and some parts of South America, sporadic cases only were reported in the United States, for instance, by GRAY in 1864 and HARRIS in 1902. I have always suspected that pellagra might be lurking unrecognised among the poorest folk in the United States, but I could hear of no trace of it during my last visit to the Eastern States in 1905, nor by correspondence with teachers of medicine. Yet in 1907-8 cases were hesitatingly reported from Alabama, South Carolina, North Carolina, and Georgia, nearly always from the lunatic asylums, and when the diagnosis had been confirmed by observers who visited Italy and London in order to confer with those who knew the disease, it became obvious that pellagra was widely prevalent in the Southern States.

It is now believed by the more senior superintendents of lunatic asylums that it has "existed in some parts of the country for over a generation." The disease has already been reported from thirty-five States, including the District of Columbia.

"While pellagra appears to be more prevalent in the South Atlantic and Gulf sections, interesting foci of the disease have been discovered in

insane asylums at Dunning and Peoria, Illinois (1909), and Philadelphia (1910), and cases of pellagra have been recognised from Massachusetts to California, and from Michigan to Texas." There are no accurate statistics as to the number of cases, but it is believed that the affected individuals during the present year are between 5,000 and 7,000. It has even been stated that in Georgia alone there are thought to be 50,000 cases! Some of the photographs, which I show you to-night by the epidiascope, were kindly sent to me by Dr. ZELLER from Peoria. The chief work in America has been done from an epidemiological point of view, as is only natural, because the observers have had to satisfy themselves that the disease which they had to treat resembled the pellagra of Italy and Egypt, and the Italian literature on the subject is so voluminous that much time has been spent in studying it. Little has been added so far to our knowledge of pellagra clinically or pathologically. There are, however, some points which should be briefly mentioned :—

1. Experience in Italy and Egypt, which are the countries where I have had an opportunity of studying more than a thousand cases of this scourge, has so far been unanimous in declaring that pellagra is almost entirely confined to the poorest classes of the rural community. But in the United States pellagra is not a disease of filth or poverty, nor is it confined to the agricultural population. I have myself been consulted (by letter) by a Louisiana physician about a well-to-do white lady, a patient of his, living in a town, who has suffered from pellagra since July, 1908.

2. It is calculated that in some of the Southern States 75 per cent. of the cases are seen among coloured women.

3. Some writers have pointed out that pellagra is often associated with considerable prevalence of amœbæ in the fæces, and have suggested that these protozoa may "act as irritants to the intestinal tract and modify its absorbability for endogenous toxines." In this connection it should not be forgotten that nearly all the pellagrous in Egypt are also victims of ankylostomiasis and bilharziasis.

4. Dr. SAMBON'S brilliant theory as to the possible causation of pellagra has of course aroused much interest in the United States, and more than one worker at the subject has embraced the opportunity of travelling in Europe with him, and of admiring the enthusiasm and tireless energy which he has displayed in studying the epidemiology of the

Fig. 1.

Pellagrous rash involving mastoid and frontal regions (bilateral). He had also symmetrical eruption on hands and wrists.

Dr. G. A. ZELLER, Peoria.

Fig. 2.

Symmetrical pellagrous erythema of neck—(also hands and forearms).

Dr. G. A. ZELLER, Peoria.

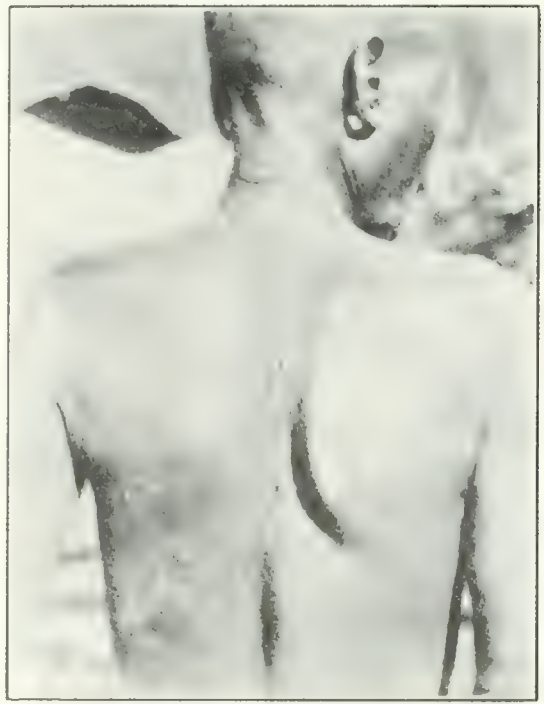

Fig. 3

A Case of Pellagra to illustrate paper by
Dr. HUGH S. STANNUS.

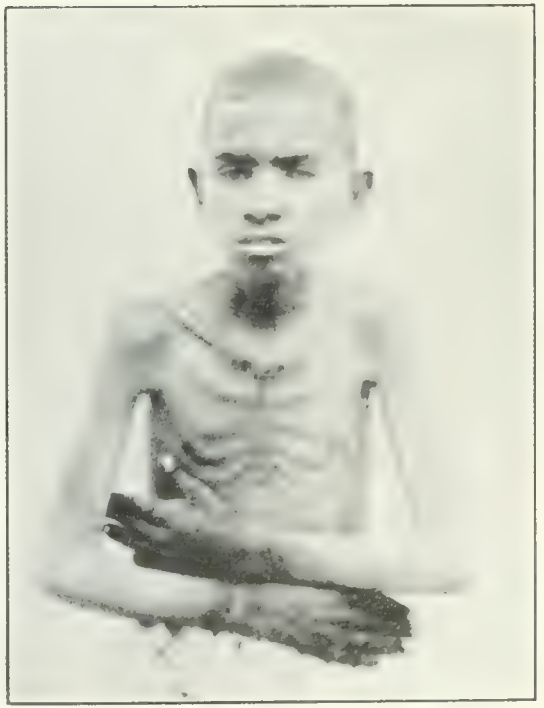

Fig. 4.

Pellagrous erythema of face, upper chest, back of hands and wrists.
Note emaciation and melancholic expression.
A peasant boy, once in Kasr el Aini Hospital, Cairo, in one of Dr. SANDWITH'S *wards.*

disease. But the monthly bulletin, published in December, 1910, by the South Carolina State Board of Health for general gratuitous distribution, sums up as follows: "When consideration is given to the various etiologic theories of pellagra and its relation to Indian corn, it is evident that the etiology of pellagra, in any definite scientific sense, is unknown. In the present state of our knowledge, however, it would seem unwise to deny entirely some causal relation between corn and pellagra. But just what this etiologic relation is, still remains to be proven" (p. 14).

"It seems that it would be wise to follow, for the present at least, in the footsteps of those who hold to the idea of some etiologic relation between corn and pellagra" (p. 24).

5. Many Fellows present to-night will remember that Dr. H. P. Cole, of Mobile, Alabama, communicated to the last British Medical Association meeting the record of thirty-one cases of pellagra, transferred directly by him by Crile's method. The patients were all "in the last stages of pellagra, or steadily retrograding under prolonged and careful treatment by approved therapeutic measures." Fifty-eight per cent. of his cases recovered, though one of them relapsed two years afterwards, apparently from re-infection. This method of treatment sounds valuable, provided the patient is not moribund and the operator possesses the necessary skill and experience.

6. During 1911, nineteen cases of pellagra, treated with salvarsan, have been reported by King and Crowell (*Jour. Amer. Med. Assoc.*, Nov. 18th, 1911, p. 1687). One patient died one month after a single dose, but the other eighteen can be claimed as apparent recoveries. Most of the patients received intravenous injections of 0·6 gramme at intervals of ten days.

Dr. Zeller states that two public-spirited citizens of New York and Washington have provided £3,000 to "finance a field expedition to study the disease at close range in the United States." In spite of the alarm which exists in some of the infected localities, there are no accurate data regarding the prevalence of the disease, for unfortunately pellagra requires to be reported in only four States, and in only one of these are such reports required by law.

Allow me to conclude this brief notice by quoting from a leading article in the *Journal of the American Medical Association* dated September 2nd, 1911: "The maize theory of the origin of the disease

appears to be attracting less attention on the part of students of the disease. SAMBON's hypothesis regarding the agency of flies of the genus *simulium* appears as yet to have few supporters in this country, although ROBERTS, of Atlanta (*Jour. Amer. Med. Assoc.*, 1911, I., p. 1713), in a recent paper, states that, from observations made in his section, conditions are very similar there to those described by SAMBON in Italy, where the disease prevails. . . . On the whole, the pellagra situation must be viewed with serious concern. . . . It therefore becomes one of the most, if not the most, important public health problem of the present."

DISCUSSION.

Dr. L. W. SAMBON: At this late hour it would be impossible to go so fully into the subject under discussion as I should wish. Besides, with regard to the recent researches which, thanks to Mr. WELLCOME's interest and generosity, I have been able to carry out in Italy, Roumania, Hungary, the Tyrol, France and Spain, it would be preferable, I think, if Dr. CHALMERS, who is present here to-night, would kindly give a short account. Dr. CHALMERS accompanied me throughout the journey and offers the great advantage of having approached the investigation with a perfectly unbiassed mind.

I must, however, express my great appreciation both of Dr. STANNUS' important paper and of Dr. SANDWITH'S able review. To Dr. STANNUS we are especially indebted for the notable contribution he has made to our knowledge of the geographical distribution of pellagra. It is now quite obvious that pellagra has a much wider range in Africa than was hitherto supposed. It was ABEILLE, a French army surgeon, who, in 1832, first recognised the disease in Africa amongst the Arab tribes of La Calle between Bone and Tunis. Then PRUNER reported it for Egypt, in 1847. DE BUCHERIE observed it in the valley of the Bou-Merzong in Algeria, in 1858. Curiously enough these and other early statements were disbelieved, and it is only since 1894, that owing to Dr. SANDWITH'S most excellent work, the great prevalence of pellagra in Egypt has been fully recognised. Quite recently, FERRER has confirmed the presence of the disease in Algeria. In 1891, MYLES reported it from

Tokar on the Red Sea. SANDWITH found it amongst coloured lunatics from South Africa on Robben Island. I have been informed that it occurs in West Africa, but the details so far supplied are insufficient for a confident diagnosis.

Dr. SANDWITH, in showing us some very interesting photographs of pellagrins, has insisted on certain diagnostic characters, such as the symmetrical distribution of the eruption. It is quite true that symmetry is the rule, but although general it is not invariable. I have seen cases in which the asymmetry was marked.

It is satisfactory to know that pellagra is now receiving the attention that it deserves. Recent work, and more especially American work, has shown that this grave disease is much more widely distributed and far more prevalent than had been imagined.

In an autopsy which we had the opportunity of making in Roumania, certain peculiar bodies were found in smears from the sensorio-motor cortex and from a blood-clot lying in contact with and posterior to the lower cervical and upper dorsal region of the spinal cord. We showed these bodies at a recent meeting of the Pellagra Investigation Committee, but, the examination of our material being yet incomplete, we were careful not to express any opinion as to the nature of these structures. To-day we find that a medical journal reports that we have discovered an organism in pellagra.

Premature information is undesirable, and it is also to be regretted that on another occasion a telegram which I had sent home was published in an incomplete and misleading form. One lives in fear and trembling of the reporter. In the discussion which followed a paper on sleeping sickness, read before the Epidemiological Society some years ago, I was made to say that not only *Glossina palpalis*, but that probably other butterflies *(sic)* might also convey to man the dread disease.

Dr. A. CHALMERS: I beg to congratulate Drs. STANNUS and SANDWITH very heartily upon the papers which they have given us. During our recent tour with Dr. SAMBON and others through Southern Europe I was much struck with the fact that when we asked in the rural districts of Hungary where cases of pellagra were likely to be found, we were invariably told we would see them in the hills, and that in the plains we would see very little of the disease. That statement was true; we

found pellagra centres were always by the streams, and in these places we always found the larvæ and pupæ of *simulium*. There was an invariable association between running water and the disease.

What is it that we regard as an endemic focus of pellagra? It is a district where young children are affected. I remember very distinctly that in a village near Bucharest, which I was told was a centre, my first request was to see the stream on which the village was situated, and I was immediately asked who had told me that most of the cases occurred near the river.

I do not forget also that we received some evidence that the disease might be associated with the eating of maize. The Roumanians who eat maize get pellagra, but the Bulgarians who do not eat maize do not get it.

It is a remarkable fact also that seasonal influences have a good deal to do with the origin of the disease, there was always much pellagra after extensive floods and inundations. Cultivation had a beneficial effect, and drainage and the cleansing of streams have in many places simultaneously abolished malaria and pellagra.

We found two popular ideas about pellagra to which reference might be made: one was that cases never occurred more than three kilometres from a stream on either side, and another that the disease was contracted by going out in the early morning during the mist.

It is impossible to make any very confident statement at present, but so far as epidemiology is concerned, Dr. SAMBON has made out a very strong case. His theory must be seriously considered and seriously worked out.

The Chairman (Sir WILLIAM LEISHMAN), in thanking the readers of the papers for their valuable and interesting contributions, said that he was glad to see how widely interest in pellagra was extending. The recognition of the existence of the disease in countries which were believed to be free from it would be the means of securing a great extension of research work directed to the determination of its etiology and prevention. If sadness of expression and inability to smile were pathognomonic features of the disease, as appeared to be suggested by some of the speakers, he was inclined to suspect that the disease might be widely prevalent in London.

Dr. Sambon and Dr. Chalmers had been good enough to show him some specimens of the bodies which they had found in some cases of pellagra, and he was quite in accord with these gentlemen in considering that they were probably of protozoal nature, though he also agreed with them in the guarded manner in which they spoke of their possible causative rôle in the disease. Their epidemiological observations were most interesting, and appeared to strengthen considerably the theory of *simulium* transmission.

CHOLERA PROPHYLAXIS IN THE DUTCH EAST INDIES.

Through the courtesy of Dr. KIEWIET DE JONGE, the Local Secretary of the Society in Java, we are enabled to publish the following interesting statistics of the results of anti-cholera vaccination which have been obtained by Dr. NYLAND, the Director of the Institut Pasteur and Vaccine Station at Batavia.

The preventive inoculations were carried out in districts where cholera is endemic, and where the disease, at certain seasons of the year, is extremely virulent and fatal. The system of work was almost entirely on a voluntary basis, and, except in the case of inmates of houses where an outbreak of cholera had occurred, no pressure was exercised on the people to undergo the treatment. The natives, however, readily availed themselves of the new prophylactic measure, and expressed themselves as highly gratified at its success.

The method of preparing the vaccine was that of KOLLE; that is to say, an emulsion of a culture of the cholera bacillus on agar was made in normal salt solution, and this was afterwards heated at 60° C. for one hour. After it had been ascertained to be sterile, a preservative was added, and the emulsion was administered in doses of 1 cc. It was found that there was no increase of immunity to cholera for five days after the vaccination, but that, on the contrary, resistance to infection was slightly lowered; after that period, however, there was a marked diminution both in the case incidence and in the fatality of the disease.

The following tables illustrate both points:—

TABLE A (NATIVES).

Samarang.

	Cholera Morbidity per mille.	Cholera Mortality per mille.
Vaccinated—		
8,340 persons	0·3	0·1
Non-vaccinated—		
85,142 persons	6·5	5·5

TABLE A—*continued.*

	Cholera Morbidity per mille.	Cholera Mortality per mille.
Singaradja.		
Vaccinated—		
4,092 persons	1·0	—
Non-vaccinated—		
115,877 persons	9·9	7·6
Den Pasar.		
Vaccinated—		
1,733 persons	1·1	1·1
Non-vaccinated—		
154,842 persons	2·9	2·7
Selong.		
Vaccinated—		
4,876 persons	0·2	—
Non-vaccinated—		
154,000 persons	5·8	3·7

EUROPEANS (BATAVIA).

The population of Batavia amounts to 10,477 Europeans. During the period from August 2nd, 1910, to June 30th, 1911, 7,279 persons were inoculated at the vaccination station under the supervision of Dr. NYLAND; of these 867 were revaccinations and 6,412 were vaccinated for the first time. Besides the inoculations at the Institut Pasteur, the doctors in the town vaccinated at least 1,200 persons, so that not fewer than 8,000 Europeans underwent the treatment.

Omitting infections which occurred during the first five days after the operation, only three cases of cholera (two of which were fatal) were observed among those inoculated, whilst of 2,500 non-vaccinated persons 112 contracted cholera in the experimental period (eleven months), and 56 of them died. In Samarang, a hotbed of cholera, not a single case occurred amongst the inoculated Europeans, and in Soerakarta also there were no fatalities.

TABLE B (EUROPEANS).

	Cholera Morbidity per mille.	Cholera Mortality per mille.
Batavia.		
Vaccinated—		
8,000 persons	0·3	0·2
Non-vaccinated—		
2,500 persons	44·0	22·0

TABLE B—*continued.*

	Cholera Morbidity per mille.	Cholera Mortality per mille.
Samarang.		
Vaccinated—		
2,450 persons	—	—
Non-vaccinated—		
2,676 persons	14·2	5·2
Soerakarta.		
Vaccinated—		
1,449 persons	3·2	—
Non-vaccinated—		
827 persons	15·7	12·0

In the village of Tengalbadan, during a severe outbreak of cholera, vaccination was commenced on a day in which there had been five deaths from the disease. The whole of the inhabitants, including old people and children, were vaccinated. With the exception of a single instance, which occurred the following day, there were no further cases of cholera.

W. C. B.

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